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(54) Title: STENT COATING

(57) Abstract: A stent having a polymeric coating for controllably releasing an included active agent. The polymeric coating includes a blend of a first polymeric material, which if alone, would release the agent at a first, higher rate, and a second polymeric material, which if alone would release the agent at a second, lower rate over a longer time period. One stent coating utilizes a faster releasing hydrophilic polymeric material and a slower releasing hydrophobic material. One stent coating includes a blend of a faster releasing PLA-PEO copolymer and a slower releasing PLA-PCL copolymer. One active agent is Taxol. One use of the Taxol delivering stent is to inhibit restenosis following angioplasty.

can be either balloon expandable or self-expanding. After angioplasty balloon dilatation, the previously constricted vessel is at least temporarily widened. A stent can be delivered on a catheter and expanded in place or allowed to expand in place against the vessel walls. With the stent in place, restenosis may or may not be inhibited, but the probability and/or degree of blockage is reduced due to the structural strength of the stent opposing the inward force of any restenosis. Restenosis may occur over the length of the stent and be at least partially opposed by the stent. Restenosis may also occur past the ends of the stent, where the inward forces of the stenosis are unopposed.

Therapeutic agents to inhibit restenosis have been used with varying success. Taxol, an antimicrotubule agent isolated from the bark of the western Pacific Yew tree, is especially effective in inhibiting some cancers and is believed to be effective in combating restenosis. Systemic administration of Taxol can have undesirable side effects, making local administration a preferred mode of treatment.

Local administration of Taxol may be more effective when carried out over a longer time period, such as a time period at least matching the normal reaction time of the body to the angioplasty. At the same time, it may be desirable to provide an initial high dosage of Taxol over an initial period. Local administration of Taxol over a period of days or even months may be most effective in inhibiting restenosis.

Controlled release of therapeutic agents can utilize various technologies. Devices are known having a monolithic layer or coating incorporating a heterogeneous solution and/or dispersion of an active agent in a polymeric substance, where the diffusion of the agent is rate limiting, as the agent diffuses through the polymer to the polymer-fluid interface and is released into the surrounding fluid. In some devices, a soluble substance is also dissolved or dispersed in the polymeric

having a first, high release rate and a second co-polymer having a second, lower release rate relative to the first release rate. The first and second copolymers are preferably erodible or biodegradable. In one embodiment, the first copolymer is more hydrophilic than the second copolymer. In one embodiment, the first copolymer includes a polylactic acid/polyethylene oxide (PLA-PEO) copolymer and the second copolymer includes a polylactic acid/polycaprolactone (PLA-PCL) copolymer.

The relative amounts and dosage rates of active agent delivered over time can be controlled by controlling the relative amounts of the faster releasing polymers relative to the slower releasing polymers. For higher initial release rates the proportion of faster releasing polymer can be increased relative to the slower releasing polymer. If most of the dosage is desired to be released over a long time period, most of the polymer can be the slower releasing polymer. The stent can be coated by spraying the stent with a solution or dispersion of polymer, active agent, and solvent. The solvent can be evaporated, leaving a coating of polymer and active agent. The active agent can be dissolved and/or dispersed in the polymer. In some embodiments, the co-polymers can be extruded over the stent body.

In use, the stent can be put into position in a body vessel such as a coronary vessel after a procedure such as angioplasty. The stent can be left in position, and the erodible or biodegradable coating allowed to degrade. As the polymeric coating degrades, the active agent can absorb into the vessel walls.

Description of the Drawings

Fig. 1 is a perspective view of a stent in accordance with an exemplary embodiment of the present invention;

Fig. 2 is a perspective view of a further preferred stent in accordance with the present invention; and

114. The areas within the rectangular wire element 114 are open 116. The rectangular wire elements 114 are aligned lengthwise in the longitudinal axis of the stent 110. Adjacent rectangular wire elements 114 are offset half the lengthwise distance of a similar rectangular wire element 114. The end of the stent is formed by the full completion of one rectangular wire element 114, and the subsequent open end of the adjacent rectangular wire element 122. Thus, the ends of the stent possess an alternating open-closed wire configuration.

These stents are exemplary of stents which may incorporate the present invention. These, and other suitable stents are disclosed in U.S. Patent Application Serial No. 08/874,190, filed June 13, 1997, entitled "Polymeric Layered Stent", of which the disclosure is incorporated herein by reference.

The term "wire", as used in describing the frame material, should not be mistaken as being limited to metallic materials. In fact, the "wire" forming the stents 10 & 110 may consist of any biocompatable material possessing the structural and mechanical attributes necessary for supporting a diseased vessel. Thus, both metallic and polymeric materials are suitable. Examples of preferred biocompatable metallic materials include stainless steel, tantalum, nitinol, and gold. Preferred polymeric materials may be selected from the list immediately below, which is not exhaustive:

poly(L-lactide) (PLLA), poly(D,L-lactide) (PLA), polyglycolide (PGA), poly(L-lactide-co-D,L-lactide) (PLLA/PLA), poly(L-lactide-co-glycolide) (PLLA/PGA), poly(D, L-lactide-co-glycolide) (PLA/PGA), poly(glycolide-co-trimethylene carbonate) (PGA/PTMC), polyethylene oxide (PEO), polydioxanone (PDS), polycaprolactone (PCL), polyhydroxylbutyrate (PHBT), poly(phosphazene), polyD,L-lactide-co-caprolactone) (PLA/PCL), poly(glycolide-co-caprolactone) (PGA/PCL), polyanhydrides (PAN),

duration of the agent is controlled to selected parameters which optimize treatment. It has been found that selected ratios of a mixture of a hydrophilic polymer and a hydrophobic polymer provide desired control of drug release.

In a preferred embodiment, the hydrophilic polymer includes a co-polymer of polylactic acid (PLA) and polyethylene oxide (PEO). In a preferred embodiment, the second polymer includes a co-polymer of polylactic acid (PLA) and poly(caprolactone) (PCL). The PLA-PEO copolymer is hydrophilic and erodes faster relative to a similar hydrophobic polymer in the body environment where the coated stent is positioned. The PLA-PCL copolymer is hydrophobic, and degrades more slowly than a comparable hydrophilic polymer. In a preferred embodiment, the polymer coating is formed of a blend of PLA-PCL and PLA-PEO. In preferred embodiments, the hydrophilic polymer has a molecular weight of greater than about 10,000 (Mn) and the second polymer has a molecular weight of greater than about 20,000 (Mn).

Formation of PLA-PEO copolymers is well known to those skilled in the art. See for example, U.S. Patent Nos. 5,476,909 and 5,548,035, herein incorporated by reference. Formation of PLA-PCL copolymers is also known to those skilled in the art. See for example, U.S. Patent No. 5,470,829, herein incorporated by reference.

One preferred embodiment includes about 20% by weight PLA-PEO and about 80% by weight PLA-PCL copolymers. Another embodiment includes about 50% by weight PLA-PEO copolymer and about 50% by weight PLA-PCL copolymer. The embodiment having about 20% PLA-PEO and 80% PLA-PCL delivers the active agent over a longer time period, but with a lower initial release, relative to the embodiment having the 50%/50% PLA-PEO/PLA-PCL combination. The relative amounts of PLA-PEO and PLA-PCL can be adjusted to achieve the desired

be accomplished using methods well known to those skilled in the art, such as mounting the stent on an inflatable balloon disposed at the distal end of a catheter. With the stent advanced into position near the dilated region, the stent can be forced outward and into position against the inner vessel walls. If the stent is self-expanding, the stent can be delivered by deploying the stent from within a delivery device, allowing the stent to expand against the inner vessel walls. The active agent, as it is released from the eroding polymeric coating, can be absorbed by the inner vessel walls. Over time, the polymeric coating is eroded by bodily fluids.

Numerous advantages of the invention covered by this document have been set forth in the foregoing description. It will be understood, however, that this disclosure is, in many respects, only illustrative. Changes may be made in details, particularly in matters of shape, size, and arrangement of parts, without exceeding the scope of the invention. The inventions's scope is, of course, defined in the language in which the appended claims are expressed.

7. A stent as recited in claim 1, wherein said first co-polymer includes PLA-PEO and said second co-polymer includes PLA-PCL.

8. A stent as recited in claim 7, wherein said agent includes an agent selected from the group consisting of paclitaxel, paclitaxel analogues, paclitaxel derivatives, and combinations thereof.

9. A stent for controllably releasing a biologically active agent over a long time period comprising:

a stent body;

a biologically active agent; and

means for adhering said agent to said stent body and controllably releasing said agent from said stent body over time, wherein said means for controllably releasing said agent includes a combination of a first means for releasing said agent at a first rate over a first time period and second means for releasing said agent at a second rate over a second time period, wherein said first rate is faster than said second rate and said first period is shorter than said second period.

10. A stent as recited in claim 9, wherein said first means for releasing includes a bioabsorbable polymeric material and second means for releasing includes a bioabsorbable polymeric material, wherein said first means is absorbed faster than said second means.

11. A stent for releasing a biologically active agent inside the human body comprising:

Fig. 1

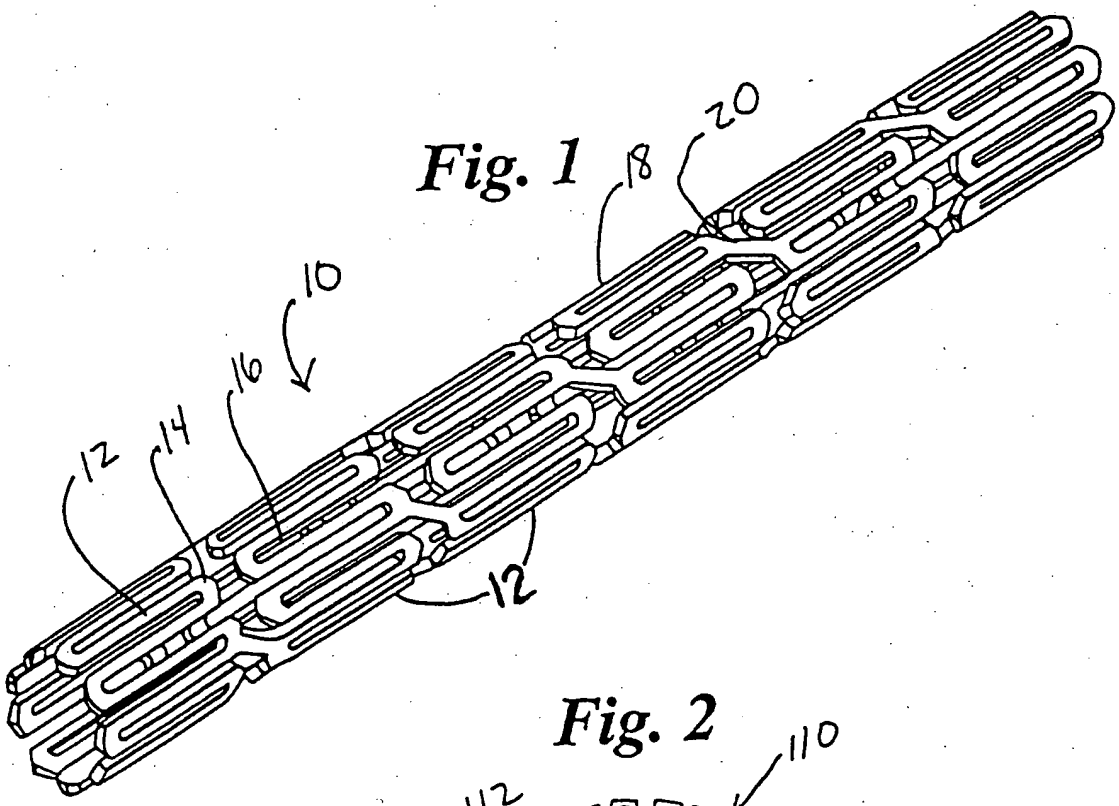
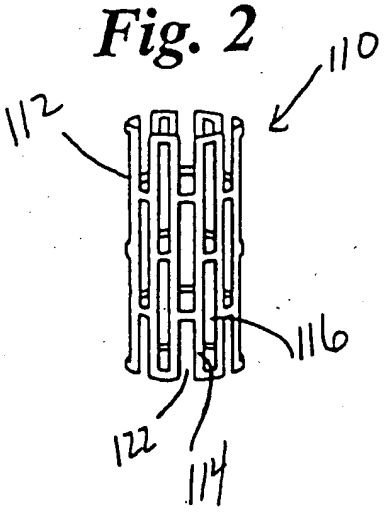


Fig. 2



INTERNATIONAL SEARCH REPORT

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PCT/US 00/40105

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/06 A61P35/00 A61K9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 56312 A (SCIMED LIFE SYSTEMS, INC.) 17 December 1998 (1998-12-17) cited in the application the whole document ---	1-13
Y	WO 99 21908 A (ANGIOTECH PHARMACEUTICALS, INC. ET AL.) 6 May 1999 (1999-05-06) page 2, line 23 -page 3, line 11 page 14, line 18 -page 20, line 5 page 50 -page 53; example 5 page 69 -page 70; example 13 --- -/--	1-13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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